elf atochem

Elf Atochem North America, Inc.
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Philadelphia, PA 19103-3222
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ORIGINAL

(A)

September 22, 1994

FEDERAL EXPRESS
RETURN RECEIPT REQUESTED

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator

Subject: TSCA Section 8(e) Submission

Contains No CBI

Dear Sir/Madam:

Elf Atochem North America Inc. is submitting the attached study to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). This study provides information on 2-Mercapto ethanol (CAS No. 60-24-2) and does not involve effects in humans. The title of the enclosed study report is 2-Mercapto Ethanol Skin Sensitization Test in Guinea-Pigs (Maximization method of Magnusson, B. and Kligman, A.M.).

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

The following is a summary of the adverse effects observed in the skin sensitization test.

2-Mercapto ethanol was tested for the potential to produce allergic skin reaction by intradermal injection and skin application to guinea pigs using a modified Magnusson and Klingman method. After challenge application, the test material produced well-defined erythema in 35% (7/20) animals and was classified as a moderate sensitizer.

11/16/94

Elf Atochem has not previously filed any 8(e) notices or Premanufacture Notifications (PMNs) on the subject material.

Results from the study report will be incorporated into the current Elf Atochem Material Safety Data Sheet for 2-mercapto ethanol.

Further questions regarding this submission may be directed to me at (215) 419-5892.

Sincerely,

C.H. Farr, PhD, DABT
Manager, Product Safety
and Toxicology

Enclosure

~~CONFIDENTIAL~~

SPONSOR
Elf Aquitaine Production
Usine de Lacq
64170 Artix
France

STUDY TITLE
SKIN SENSITIZATION TEST IN GUINEA-PIGS (Maximization method of Magnusson, B. and Kligman, A.M.)

TEST SUBSTANCE
2-MERCAPTO ETHANOL

STUDY DIRECTOR
Jack Clouzeau

STUDY COMPLETION DATE
16th June 1994

PERFORMING LABORATORY
Centre International de Toxicologie (C.I.T.)
Miserey - 27005 Evreux - France

LABORATORY STUDY NUMBER
11595 TSG

Contains No CBI

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with the principles of Good Laboratory Practice Regulations:
. O.E.C.D. Principles of Good Laboratory Practice, C(81)30(final) Annex 2. May 12, 1981.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at the Centre International de Toxicologie (C.I.T.), Miserey, 27005 Evreux, France.

Toxicology

J. Clouzeau Date: 16.6.94
Study Director
Biologist

OTHER SCIENTISTS INVOLVED IN THIS STUDY

For Pharmacy: J. Richard
Doctor of Pharmacy

For Toxicology: C. Pelcot
Study Supervisor

STATEMENT OF QUALITY ASSURANCE UNIT

1. Specific study inspections

Type of inspections	Dates (day/month/year)	
	Inspections	Report to Study Director / Management (*)
Protocol	8.3.94	8.3.94
Report	3.6.94	6.6.94

2. Routine inspections performed on other studies of the same type according to a frequency defined in Q.A.U. procedures

Inspected phase	Dates (day/month/year)	
	Inspections	Report to Study Director / Management (*)
Test substance/preparation	3.12.93	7.12.93
Treatment/Test substance	14.1.94	17.1.94
Animals/housing	21.1.94	24.1.94

The inspections were performed in compliance with C.I.T. Quality Assurance Unit procedures and the Good Laboratory Practice Regulations.

(*) The dates mentioned correspond to the dates of signature of audit reports by Study Director / Management.

M. Labiche Date: 16.6.94
Pharmacist
Head of Quality Assurance Unit
and Scientific Archives

SUMMARY

At the request of Elf Aquitaine Production, Artix, France, the potential of the test substance, 2-MERCAPTO ETHANOL, to induce delayed contact hypersensitivity following intradermal injection and cutaneous application was evaluated in guinea-pigs according to the maximization method of Magnusson and Kligman. The study was conducted in compliance with the Principles of Good Laboratory Practice Regulations.

Methods

Thirty guinea-pigs (15 males and 15 females) were allocated to 2 groups: a control group 1 (5 males and 5 females) and a treated group 2 (10 males and 10 females).
The sensitization potential of the test substance was evaluated after a 10-day induction period during which time the animals were treated with isotonic aqueous NaCl solution (control group) or the test substance (treated group). On day 1, in presence of Freund's complete adjuvant, 0.1 ml of the test substance at a concentration of 0.1% (w/w) in the vehicle was administered by intradermal route. On day 8, 0.5 ml of the test substance at a concentration of 10% (w/w) in the vehicle was applied by cutaneous route during 48 hours by means of an occlusive dressing. After a period of 12 days without treatment, a challenge cutaneous application of 0.5 ml of the vehicle (left flank) and 0.5 ml of the test substance at a concentration of 25% (w/w) in the vehicle (right flank) were administered to all animals. The test substance and the vehicle were prepared on a dry compress then applied to the skin and held in place for 24 hours by means of an occlusive dressing. Cutaneous reactions on the challenge application sites were then evaluated 24 and 48 hours after removal of the dressing.

After the final scoring period, the animals were sacrificed and cutaneous samples were taken from the challenge application sites from all the animals. No histological examination was performed on the cutaneous samples.

The sensitivity of the guinea-pigs in C.I.T. experimental conditions were checked in a recent study with a positive sensitizer: Dinitro 2.4 Chlorobenzene. During induction period the test substance was applied at 0.05% (day 1) and 0.5% (day 8) concentrations. At cutaneous challenge application, 0.1% and 0.5% were tested on both flanks.

Results

No clinical signs and no deaths were noted during the study.

After 24 hours following removal of the dressing of the cutaneous challenge application of the test substance, clearly visible cutaneous reactions attributable to sensitization were recorded in 7 animals of the treated group. In addition and in the absence of cutaneous reactions in the control group, the very slight erythema observed after 24 and 48 hours in 1 animal was considered as attributable to sensitization.

The guinea-pigs which were used in a recent study showed a satisfactory sensitization response in 100% animals using a positive sensitizer (appendix 5).

Conclusion

Under our experimental conditions and according to the maximization method established by Magnusson and Kligman, cutaneous reactions attributable to the sensitization potential of the test substance, 2-MERCAPTO ETHANOL, at the concentration of 25%, were observed in 40% guinea-pigs. The allergenicity level is III, moderate

1. INTRODUCTION

The objective of this study, performed according to maximization method established by Magnusson and Kligman (1), was to evaluate the potential of the test substance, 2-MERCAPTO ETHANOL, to induce delayed contact hypersensitivity in guinea-pigs.

The results of the study are of value in predicting the contact sensitization potential of the test material in Man.

During the induction period, the test substance was administered by intradermal route (together with an adjuvant to maximise potential reactions) and cutaneous route. After a rest period of 12 days, a challenge application with the test substance was performed in order to provoke a cutaneous sensitization reaction.

The study was conducted in compliance with:
. O.E.C.D. guideline No. 406, 17th July 1992.

(1) Magnusson, B.; Kligman, A.M.: The identification of contact allergens by animal assay. The guinea-pig maximization test. J. Invest. Derm. 52: 268-276 (1969).

2. MATERIALS AND METHODS

2.1. TEST AND CONTROL SUBSTANCES

2.1.1 Test substance

The test substance, 2-MERCAPTO ETHANOL, used in the study was supplied by Elf Aquitaine Production.

Documentation supplied by the Sponsor identified the test substance as follows:
. denomination:
  - protocol: 2-MERCAPTO ETHANOL
  - labelling: MERCAPTO 2 ETHANOL N° d'archivage au CAL : 1026/93
. batch number:
  - protocol: T 60260-ME
  - labelling: T 60260-ME
. description: colourless liquid
. container: 1 glass flask
. date of receipt: 25.5.93
. storage conditions: at room temperature, protected from light
. purity: 99.85%

Data relating to the characterization of the test substance are documented in a test article description and a test article analysis (presented in appendix 1) provided by the Sponsor.

2.1.2 Vehicle

The vehicle used was sterile isotonic aqueous NaCl solution, batch No. 3067 (Biosédra, 92240 Malakoff, France).

2.1.3 Other substances

The other substances used were:
. Freund's complete adjuvant, batch No. 29829 (Osi, 75739 Paris, France);
. sodium laurylsulphate, batch No. 33H1306 (Sigma, 38070 Saint-Quentin-Fallavier, France);
. vaseline, batch Nos. 0013 and 0015 (Coopérative Pharmaceutique Française, 77000 Melun, France).

2.2. TEST SYSTEM

2.2.1 Animals

Species and strain: Dunkin-Hartley guinea-pigs.
Reason for this choice: species recommended by the international regulations for sensitization studies. The strain used has been shown to produce a satisfactory sensitization response using known positive sensitizers.
Breeder: Centre d'Elevage Lebeau, 78950 Gambais, France.
Number: 30 animals (15 males and 15 females).
Allocation of the animals to the groups: on day -1, the animals were weighed and randomly allocated to 2 groups: a control group 1 consisting of 10 animals (5 males and 5 females) and a treated group 2 consisting of 20 animals (10 males and 10 females).
Weight: on day 1, the animals had a mean body weight of 328 ± 18 g for the males and 343 ± 21 g for the females.
Acclimatization: at least 5 days before the beginning of the study.
Identification of the animals: the animals were identified individually by an ear-tattoo.

2.2.2 Environmental conditions

During the acclimatization period and throughout the study, the conditions in the animal room were as follows:
. temperature: 22 ± 3°C
. relative humidity: 30 to 70%
. light/dark cycle: 12 h/12 h
The air was non-recycled and filtered.
During the acclimatization period and throughout the study, the animals were housed individually in polycarbonate cages (48 x 27 x 20 cm) equipped with a polypropylene bottle. Sifted and dusted sawdust was provided as litter (SICSA, 92142 Alfortville, France). An analysis of potential residues and major contaminants is performed periodically (Laboratoire Wolff, 92110 Clichy, France).

2.2.3 Food and water

During the study, the animals had free access to "Guinea-pigs sustenance reference 106 diet" (U.A.R., 91360 Villemoisson-sur-Orge, France).
Food was periodically analysed (composition and contaminants) by the supplier.
The diet formula is presented in appendix 2.

Drinking water filtered by a F.G. Millipore membrane (0.22 micron) was contained in bottles.
Bacteriological and chemical analysis of the water and detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed periodically.
Results are archived at C.I.T.

There were no contaminants in the diet, water or sawdust at levels likely to have influenced the outcome of the study.

2.3. TREATMENT

2.3.1 Preliminary test

A preliminary test taking into account the toxicity of the test substance was performed to define the concentration to be tested in the main study.

By intradermal route
Determination of the Minimum Irritant Concentration (M.I.C.):
. 24 hours before treatment, the dorsal region of the animals was clipped,
. the test substance was prepared in an appropriate vehicle,
. intradermal administration of the test substance (volume 0.1 ml) at increasing concentrations was performed in order to determine the maximum concentration which does not cause necrosis or ulceration, but an irritation,
. evaluation of the potential cutaneous reactions, 24 and 48 hours after injection.

By cutaneous route
Determination of the Minimum Irritant Concentration (M.I.C.) and Maximum Non-Irritant Concentration (M.N.I.C.):
. 24 hours before treatment, the dorsal region of the animals was clipped,
. the test substance was diluted in an appropriate vehicle,
. 0.5 ml of each concentration was applied to a gauze patch of approximately 4 cm^2 and then held in place by an occlusive dressing for 24 hours,
. potential cutaneous reactions were evaluated 24 hours after removal of the gauze patches.

2.3.2 Main study

2.3.2.1 Preparation of the animals

For all animals and before each treatment, the application sites were:
. clipped on days -1 and 7 (scapular area 4 cm x 2 cm),
. clipped again on days 21 and 25 (each flank 2 cm x 2 cm)
. shaved on day 21.

2.3.3 Induction phase by intradermal and cutaneous routes

2.3.3.1 Intradermal route

On day 1, 6 intradermal injections were made into a clipped area (4 cm x 2 cm) in the scapular region, using a needle (diameter: 0.50 x 16 mm, Terumo: C.M.L., 77140 Nemours, France) mounted on a 1 ml glass syringe (0.01 ml graduations, Record: Carrieri, 75005 Paris, France). Three injections of 0.1 ml were injected into each side of the animal, as follows:

Control group (figure 1)
. Freund's complete adjuvant diluted to 50% (v/v) with an injectable isotonic solution (NaCl 0.9%),
. vehicle,
. a mixture of 50/50 (w/v) Freund's complete adjuvant diluted to 50% (v/v) with a sterile isotonic aqueous NaCl solution and the vehicle.

Treated group (figure 2)
. Freund's complete adjuvant diluted to 50% (v/v) with a sterile isotonic aqueous NaCl solution,
. test substance at a concentration of 0.1% (w/w) in the vehicle,
. a mixture 50/50 (w/v) of Freund's complete adjuvant diluted to 50% (v/v) with a sterile isotonic aqueous NaCl solution, and, the test substance at a concentration of 0.1% (w/w) in the vehicle.

2.3.3.2 Cutaneous route

On day 7, the scapular area was clipped. As the test substance is shown to be non-irritant after occlusive cutaneous treatment during preliminary test, the animals were treated with 0.5 ml of sodium laurylsulphate (10%) in vaseline to provoke local irritation.

On day 8, a cutaneous application on the 6 injection areas (4 cm x 2 cm) of the scapular region was performed.
Control group
. application of 0.5 ml of the vehicle.

Treated group
. application of 0.5 ml of the test substance at 10% (w/w) in the vehicle.

The test substance and the vehicle were prepared on a dry compress (Semes France, 54183 Heillecourt, France), which was then applied to the scapular region and held in place for 48 hours by means of an adhesive hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).

No residual test substance was observed at removal of the dressing.
One hour after removal of the occlusive dressing, cutaneous reactions were recorded.

2.3.3.3 Challenge phase

At the end of the rest period on day 22, the test substance was applied at the Maximum Non-Irritant Concentration (M.N.I.C.) i.e. at a concentration of 25% (w/w) in the vehicle.

On day 22, the animals from both groups received an application of 0.5 ml of the M.N.I.C. of the test substance on the posterior right flank, and 0.5 ml of the vehicle on the posterior left flank. This application was performed using a 1 ml plastic syringe (0.01 ml graduations, Terumo: C.M.L., 77140 Nemours, France). The test substance and the vehicle were prepared on a dry compress (Semes France, 54183 Heillecourt, France), then applied to a 4 cm^2 (2 cm x 2 cm) clipped area of the skin. The compress was held in contact with the skin for 24 hours by means of an occlusive, hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).

No residual test substance was observed at removal of the dressing.

2.4. SCORING OF CUTANEOUS REACTIONS

Twenty-four and 48 hours after removal of the dressing from the challenge application site, the both flanks of the treated and control animals were observed in order to evaluate cutaneous reactions, according to the following scale:

Erythema and eschar formation

. No erythema 0
. Very slight erythema (barely perceptible) 1
. Well-defined erythema 2
. Moderate to severe erythema 3
. Severe erythema (beet redness) to slight eschar formation (injuries in depth)..... 4

Oedema formation

. No oedema 0
. Very slight oedema (barely perceptible) 1
. Slight oedema (visible swelling with well-defined edges) 2
. Moderate oedema (visible swelling raised more than 1 millimetre) 3
. Severe oedema (visible swelling raised more than 1 millimetre and extending beyond the area of exposure)..... 4

Any other lesions were noted.

2.5. CLINICAL EXAMINATIONS

The animals were observed twice a day during the study in order to record clinical signs and to check for mortality.

2.6. BODY WEIGHT

The animals were weighed individually on the day of allocation into the groups, on the first day of the study (day 1), then on days 8, 15 and 25.

2.7. PATHOLOGY

2.7.1 Necropsy

On day 25, after the 48-hour observation period, the animals were sacrificed by CO_2 inhalation in excess.

2.7.2 Cutaneous samples

On day 25, a skin sample was taken from the treatment sites of the posterior left and right flanks of all animals. The samples were preserved in 10% buffered formalin.

2.7.3 Microscopic examination

No histological examinations were performed.

2.8. DETERMINATION OF THE ALLERGENICITY LEVEL

The treated animals show a positive reaction if macroscopic cutaneous reactions are clearly visible (erythema and/or oedema ≥ 2) and more marked than the most severe reactions of the control animals.

Determination of the allergenicity level
The allergenicity level of the test substance is calculated by comparing the number of animals showing positive reactions with the number of surviving treated animals at the end of the study.

% of animals showing a reaction	Allergenicity level	Classification
0 - 8	I	very weak
9 - 28	II	weak
29 - 64	III	moderate
65 - 80	IV	strong
81 - 100	V	very strong

According to the E.E.C. directive 91/325/E.E.C. published in the Journal Officiel des Communautés Européennes, when the reactions are positive in at least 30% of the treated animals, the test substance has sensitization properties and the sentence "R 43: May cause sensitization by skin contact" must be applied.

2.9. SUMMARY DIAGRAMS

Figure 1: control group

Chronology

Day -1 Clipping of the scapular region

Day 1 Intradermal injection

Day 7 Clipping + Sodium laurylsulphate

Day 8 Application covered by an occlusive dressing

Day 10 Removal of dressing and scoring after one hour

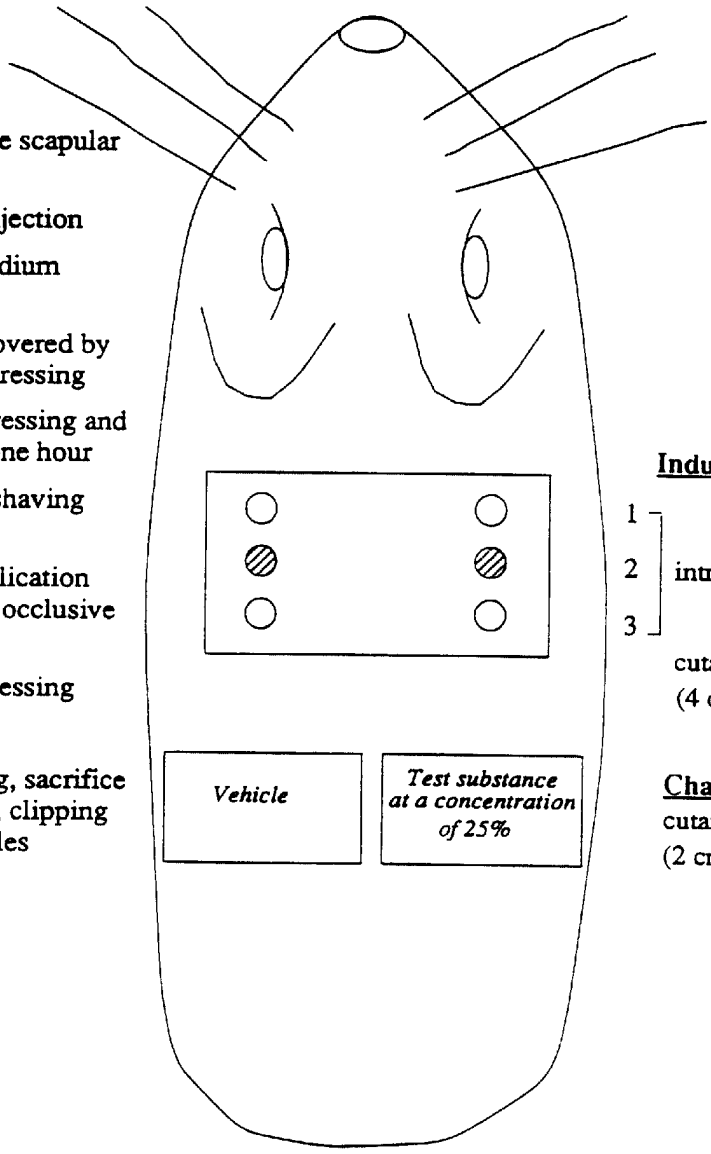
Day 21 Clipping and shaving of the flanks

Day 22 Challenge application covered by an occlusive dressing

Day 23 Removal of dressing

Day 24 First scoring

Day 25 Second scoring, sacrifice of the animals, clipping and skin samples



Intradermal injections

1 - 50% Freund's complete adjuvant and NaCl 0.9% solution

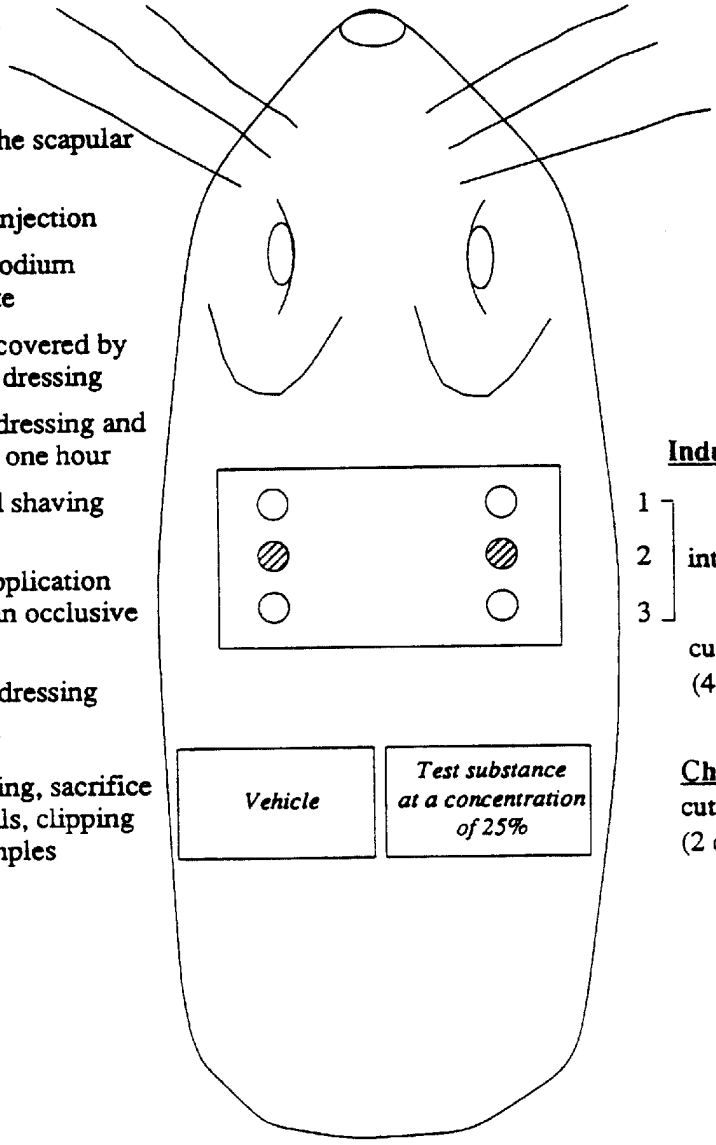
2 vehicle

3 - 1 + 2, 50/50 (w/v)

Figure 2: treated group

Chronology

Day -1	Clipping of the scapular region
Day 1	Intradermal injection
Day 7	Clipping + Sodium laurylsulphate
Day 8	Application covered by an occlusive dressing
Day 10	Removal of dressing and scoring after one hour
Day 21	Clipping and shaving of the flanks
Day 22	Challenge application covered by an occlusive dressing
Day 23	Removal of dressing
Day 24	First scoring
Day 25	Second scoring, sacrifice of the animals, clipping and skin samples



Intradermal injections

○	1	50% Freund's complete adjuvant and NaCl 0.9% solution
▨	2	test substance and vehicle (w/w)
○	3	1 + 2, 50/50 (w/v)

2.10. CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date	Day
Arrival of the animals	3.3.94	-8
Allocation of the animals into groups	10.3.94	-1
Weighing, induction by intradermal injection	11.3.94	1
Laurylsulfate application	17.3.94	7
Weighing, induction by cutaneous route	18.3.94	8
Removal of occlusive dressings and scoring of local reactions after 1 hour	20.3.94	10
Weighing	25.3.94	15
Challenge cutaneous application	1.4.94	22
Removal of occlusive dressings	2.4.94	23
Scoring of cutaneous reactions after . 24 hours . 48 hours	3.4.94 4.4.94	24 25
Weighing, sacrifice of the animals and skin samples	4.4.94	25

2.11. ARCHIVES

The study archives:
. protocol and possible amendments,
. raw data,
. correspondence,
. final study report and possible amendments,

are stored in the premises of C.I.T., Miserey, 27005 Evreux, France, for 5 years after the end of the *in vivo* study. At the end of this period, the study archives will be returned to the Sponsor.

3. RESULTS

3.1. PRELIMINARY STUDY

3.1.1 Administration by intradermal route

Several tests were performed to determine the minimal irritant concentration which did not provoke necrosis or ulceration.

Animal number	Concentration of the test substance % (w/w)	Scoring after treatment 24 hours	48 hours
Male 01 / Female 01	0.1	Irritation	Irritation
	1.0		
Male 02 / Female 02	5	Irritation	Necrosis

M.I.C. is ≥ 1.0%

Concentration used in the main study is 0.1%(w/w) of the test substance to take into account that the test substance was toxic by dermal route.

3.1.2 Application by cutaneous route

Several tests were performed to determine the M.I.C. and the M.N.I.C. after application of the test substance covered by an occlusive dressing for 24 hours.

Animal number	Concentration of the test substance % (w/w)	Scoring 24 hours after removal of the dressing (1) E	O
Males 01, 02	10	0	0
Females 01, 02	25	0	0

M.I.C. was not determined.
E: erythema
O: oedema

(1) No residual was observed.

As the test substance was anticipated to be toxic by cutaneous route, the concentration of 10% (w/w) was applied during the induction period to the intradermal injection sites, and the concentration of 25% (w/w) was tested at challenge application.

3.2. MAIN STUDY

3.2.1 Clinical examinations

No clinical signs or mortalities were observed during the study.

The body weight gain of the treated animals was normal when compared to that of the control animals (figures 3 and 4, appendix 3).

3.2.2 Scoring of cutaneous reactions (appendix 4)

3.2.2.1 End of the induction period

On day 10, after removal of the dressing, irritation in control and treated groups were observed at the intradermal injection sites.

3.2.2.2 Challenge application

After the challenge application, a very slight (score of 1), well-defined (score of 2) erythema was observed at the following frequency:

Erythema

Groups	Sex	Erythema score	Scoring of the cutaneous parameters			
			24 hours		48 hours	
			LF	RF	LF	RF
Control 1	Male	0	5/5	5/5	5/5	5/5
Treated 2	Male	0	10/10	-	10/10	7/10
		1	-	6/10	-	3/10
		2	-	4/10	-	-
Control 1	Female	0	5/5	5/5	5/5	5/5
Treated 2	Female	0	10/10	1/10	10/10	8/10
		1	-	6/10	-	2/10
		2	-	3/10	-	-

LF: left flank (control)
RF: right flank (treated)

No oedema was observed.
A dryness of the skin on the right flank was observed after 48 hours in 15/20 animals of the treated group.

4. DISCUSSION

In the absence of cutaneous reactions in the control group, the very slight erythema noted after 24 and 48 hours in 1 animal (No. 147) and the clearly visible reactions noted after 24 hours in 7 animals (Nos. 150, 152, 153, 155, 167, 169, 170) were considered as attributable to sensitization.

Figure 3: Male body weight gain (g)

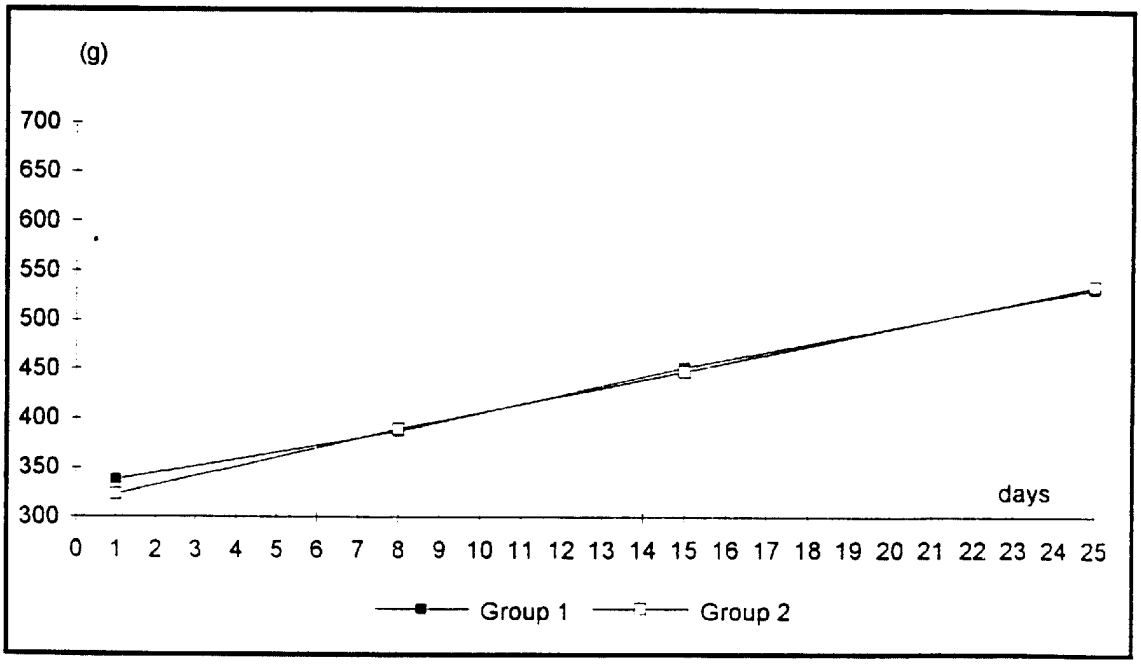
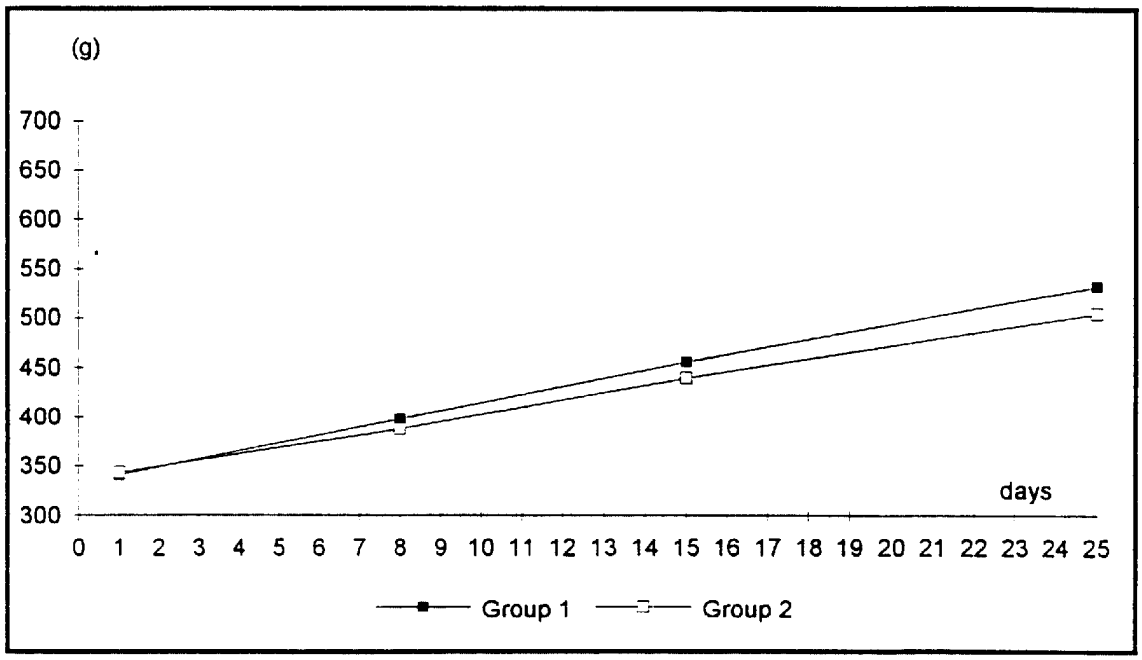


Figure 4: Female body weight gain (g)



APPENDICES

1. Test article description and certificate of analysis

TOXICOLOGY DEPARTMENT
CONFIDENTIAL
1er March 1993

elf atochem s.a.
La défense 10; cedex 42
92091 Paris-la-Défense, France

TEST ARTICLE DESCRIPTION

2-MERCAPTOETHANOL

STRUCTURAL FORMULA

$HO\text{-}CH_2\text{-}CH_2\text{-}SH$

IDENTITY

Test article name	:	2-mercaptoethanol
Chemical name	:	Ethanol-1, thiol-2
CAS number	:	60-24-2
EINECS number	:	2004646
Molecular formula	:	C_2H_6OS
Molecular weight	:	78.13
Purity	:	99.85% (w/w)
Origin and batch	:	SNEA(P), T 60260-ME
Elf Atochem filing number	:	CAL 1026/93

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	Colorless liquid
Viscosity	:	3.4 mPa.s at 20°C
Specific gravity	:	1.116 at 20°C
Melting point	:	-100°C
Boiling point	:	157-158°C at 760 mm Hg
Vapor pressure	:	1.24-1.33 mbar at 20°C
		11 mbar at 50°C
Flash point	:	76.7°C (open cup)
Solubility	:	Soluble in water

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

LD50 / Oral / Rat = 300 mg/kg. LD50 / Dermal / Rabbit = 150 mg/kg. Irritating for skin and eyes.

STORAGE AND DISPOSAL

Storage	:	In dark and at room temperature
Expiry date	:	March 1994
Disposal	:	Incineration

elf aquitaine production

adresse postale :
BP 22 64170 Lacq
téléphone : - 33 - 59 92 22 22
télex : pétra 560053F

direction exploration production france

CENTRE ATOCHEM LEVALLOIS
95 rue DANTON
92303 LEVALLOIS-PERRET

FRANCE
A l'attention de M. BOURALY

v/réf.

n/réf. 93_6003

objet : ANALYSE du MERCAPTO 2 ETHANOL (M2E)
LOT T60260 ME

CARACTERISTIQUES		ANALYSES
Pureté	(%Pds)	99.85

Lacq, le 15 Février 1993

M. DELOURME R.

2. Diet formula

Ref: 106

COMPLETE DIET

GUINEA-PIG MAINTENANCE DIET

Appearance: 4.5 mm diameter granules

Conditioning: bags of 25 kgs

Daily portion: Guinea-pigs 35-50 g, water *ad libitum*.

FORMULA %

Cereals	42
Grain biproducts and legumes	46
Vegetable protein (soya bean meal, yeast)	9
Vitamin and mineral mixture	3

AVERAGE ANALYSIS %

Calorific value (KCal/kg)	2600
Moisture	10
Proteins	17
Lipids	3
Carbohydrates (N.F.E.)	49
Fibre	13
Minerals (ash)	8

AMINO ACID VALUES
(calculated in mg/kg)

Arginine	8500
Cystine	2500
Lysine	7200
Methionine	2100
Tryptophan	2000
Glycine	6000

FATTY ACID VALUES
(calculated in mg/kg)

Palmitic acid	3600
Palmitoleic acid	0
Stearic acid	700
Oleic acid	5900
Linoleic acid	11200
Linolenic acid	3000

MINERALS (calculated in mg/kg)

	Nat. val.	CMV val.	Total
P	7400	1400	8800
Ca	5400	5600	11000
K	12000	0	12000
Na	1300	1950	3250
Mg	3270	130	3400
Mn	60	40	100
Fe	170	150	320
Cu	10	15	25
Zn	40	45	85
Co	0.1	1.5	1.6
I	0	0	0
Cl	0	0	0

VITAMINS (calculated per kg)

	Nat. val.	CMV val.	Total
Vitamin A	3500 IU	7500 IU	11000 IU
Vitamin D3	30 IU	2000 IU	2030 IU
Vitamin B1	6 mg	6.4 mg	12.4 mg
Vitamin B2	5 mg	6.4 mg	11.4 mg
Vitamin B3	22 mg	26 mg	48 mg
Vitamin B6	0.7 mg	2.7 mg	3.4 mg
Vitamin B12	0.003 mg	0.012 mg	0.015 mg
Vitamin C	0 mg	400 mg	400 mg
Vitamin E	15 mg	60 mg	75 mg
Vitamin K3	5 mg	12.6 mg	17.6 mg
Vitamin PP	97 mg	14.5 mg	111.5 mg
Folic acid	2.2 mg	1.3 mg	3.5 mg
P.A.B. acid	0 mg	2.5 mg	2.5 mg
Biotin	0.02 mg	0.06 mg	0.08 mg
Choline	1010 mg	60 mg	1070 mg
Meso-Inositol	0 mg	62.5 mg	62.5 mg

This food is supplemented with stabilized coated vitamin C, avoiding the need of other food substances (greenery, ascorbic acid) if used within 4 months of date of manufacture.

U.A.R., 7 rue Galliéni, 91360 Villemoisson - Tel: 69.04.03.57 - Fax : 69.04.81.97
(Ref. Doc. UAR: 1992)

3. Individual body weight values

INDIVIDUAL BODY WEIGHT VALUES
(g)

Groups	Sex	Animals	Days							
			-1	1	(1)	8	(1)	15	(1)	25
1	Male	141	330	337	55	392	55	447	74	521
		142	322	346	59	405	56	461	86	547
		143	351	378	29	407	58	465	71	536
		144	312	324	63	387	61	448	94	542
		145	306	307	39	346	93	439	80	519
		M	324	338	49	387	65	452	81	533
		SD	18	27	14	25	16	11	9	13
	Female	156	349	355	77	432	55	487	77	564
		157	329	335	57	392	72	464	80	544
		158	327	340	41	381	61	442	85	527
		159	304	317	63	380	52	432	85	517
		160	358	358	47	405	49	454	54	508
		M	333	341	57	398	58	456	76	532
		SD	21	17	14	22	9	21	13	22
2	Male	146	316	324	53	377	71	448	70	518
		147	305	324	44	368	65	433	78	511
		148	344	339	79	418	72	490	106	596
		149	330	320	60	380	63	443	85	528
		150	321	322	63	385	33	418	107	525
		151	320	320	90	410	59	469	95	564
		152	310	313	87	400	79	479	90	569
		153	310	319	59	378	62	440	89	529
		154	351	340	70	410	36	446	79	525
		155	307	313	57	370	43	413	79	492
		M	321	323	66	390	58	448	88	536
		SD	16	9	15	18	16	25	12	31
	Female	161	332	327	32	359	53	412	58	470
		162	334	328	46	374	36	410	68	478
		163	318	322	50	372	50	422	50	472
		164	320	325	29	354	47	401	37	438
		165	312	316	46	362	49	411	57	468
		166	352	355	24	379	64	443	61	504
		167	368	369	66	435	58	493	81	574
		168	378	385	40	425	49	474	80	554
		169	355	362	33	395	58	453	77	530
		170	341	349	74	423	52	475	82	557
		M	341	344	44	388	52	439	65	505
		SD	22	23	16	30	8	33	15	46

(1) = Body weight gain
M = Mean
SD = Standard Deviation

4. Individual observation of cutaneous reactions

MACROSCOPIC EXAMINATION OF CUTANEOUS REACTIONS

Challenge application

Group	Sex	Animals	Day 24 scoring period (after 24 hours)				Day 25 scoring period (after 48 hours)			
			Erythema		Oedema		Erythema		Oedema	
			LF	RF	LF	RF	LF	RF	LF	RF
Control 1	Male	141	0	0	0	0	0	0	0	0
		142	0	0	0	0	0	0	0	0
		143	0	0	0	0	0	0	0	0
		144	0	0	0	0	0	0	0	0
		145	0	0	0	0	0	0	0	0
	Female	156	0	0	0	0	0	0	0	0
		157	0	0	0	0	0	0	0	0
		158	0	0	0	0	0	0	0	0
		159	0	0	0	0	0	0	0	0
		160	0	0	0	0	0	0	0	0
Treated 2	Male	146	0	1	0	0	0	0	0	0
		147	0	1	0	0	0	1	0	0
		148	0	1	0	0	0	0/S	0	0
		149	0	1	0	0	0	0	0	0
		150	0	2	0	0	0	1/S	0	0
		151	0	1	0	0	0	0/S	0	0
		152	0	2	0	0	0	0/S	0	0
		153	0	2	0	0	0	1/S	0	0
		154	0	1	0	0	0	0	0	0
		155	0	2	0	0	0	0/S	0	0
	Female	161	0	0	0	0	0	0	0	0
		162	0	1	0	0	0	0/S	0	0
		163	0	1	0	0	0	0/S	0	0
		164	0	1	0	0	0	0/S	0	0
		165	0	1	0	0	0	0/S	0	0
		166	0	1	0	0	0	0/S	0	0
		167	0	2	0	0	0	1/S	0	0
		168	0	1	0	0	0	0/S	0	0
		169	0	2	0	0	0	1/S	0	0
		170	0	2	0	0	0	0/S	0	0

LF: left flank (control)
RF: right flank (treated)
S: dryness of the skin

5. Positive control to check the sensitivity of Dunkin-Hartley guinea-pigs

Purpose: check the sensitivity of Dunkin-Hartley guinea-pigs to a positive control test article

Method	:	Magnusson and Kligman	
Test substance	:	DINITRO 2.4 CHLOROBENZENE	
C.I.T. Study - Date	:	January 1994 (CIT/Study No. 11284 TSG)	
Number of animals	:	5 females	
Induction	:	0.05%	intradermal route day 1
		0.5%	cutaneous route day 8
Challenge application	:	0.1%	right flank
		0.5%	left flank

Conclusion

Under our experimental conditions and according to the Magnusson and Kligman method, DINITRO 2.4 CHLOROBENZENE at a concentration of 0.5% induced positive skin sensitization reactions in 100% of the guinea-pigs.

INDIVIDUAL REACTIONS: CHALLENGE PHASE
MACROSCOPIC FINDINGS

Group	Sex	Animals	24-hour scoring period				48-hour scoring period				Conclusion	
			Erythema		Oedema		Erythema		Oedema			
			LF	RF	LF	RF	LF	RF	LF	RF	LF	RF
Treated	Female	76	2	1	0	0	2/S	1/S	0	0	+	+/-
		77	2/S	1/S	0	0	2/S	2/S	0	0	+	+
		78	3	2	2	2	3/S	2/S	0	0	+	+
		79	4/S	2/S	2	0	4/A	2/S	0	0	+	+
		80	2/S	1	0	0	2/S	1/S	0	0	+	+/-

+/-: borderline
+ : hypersensitizing reaction
S : dryness of the skin
A : crust
LF: left flank
RF: right flank

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 15 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and **refer to the reverse side of this page for "EPA Information Requests"** .

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EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 13209A

Triage of 8(e) Submissions

Date sent to triage: AUG 22 1985

NON-CAP CAP

Submission number: 8EHQ-0885-0132

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

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entire document: 0 1 2 **pages** 1,2 **pages** 1,2, TAB

Notes:

Contractor reviewer : PR **Date:** 12/7/94

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0994 -13209 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Elf Atochem North America, Inc.

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER PROTECTION
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/22/94 [redacted] DATE: 09/27/94 CSRAD DATE: 11/16/94

CHEMICAL NAME: CAS#

60-24-2

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	(0243)	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	(0228)	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA: NON-CBI INVENTORY

(YES)
CAS SR NO
IN TRIAGE

ONGOING REVIEW

YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES

GP

TOXICOLOGICAL CONCERN:

LOW
(MED)
HIGH

USE:

PRODUCTION:

13209A

M

Dermal sensitization in guinea pigs is of moderate concern. The compound was tested for its potential to cause delayed contact hypersensitivity following intradermal injection and skin application to guinea pigs (10/sex) using a modified Magnusson and Kligman method. Following a 10-day induction period, animals were challenged with the compound; well-defined erythema was observed in 35% (7/20).